

REMARKS

Claims 1-6 are all of the claims pending in the application. Claims 1-6 are cancelled herein without prejudice or disclaimer and new Claims 7-20 are added.

New independent Claims 7,8, 11-14, and 16-17 correspond to cancelled Claims 1-6, amended as described below. New dependent Claims 9, 10, 15, and 18-20 are directed to particular preferred embodiments of the invention.

**I. Rejection of claims under 35 U.S.C. § 112**

Claims 1-6 are rejected under 35 U.S.C. § 112, second paragraph.

a. Claims 1-4 are each rejected as being indefinite in the recitation "multiple kinds of biomolecules" because it is allegedly unclear whether each array comprises more than one kind of "biomolecule," e.g., whether the claims encompass both proteins and nucleic acids on the same array.

The Examiner's suggestion that the phrase "kinds of biomolecules" be replaced with the phrase "sequences of oligonucleotides" is gratefully acknowledged. However, Applicants respectfully draw the Examiner's attention to, for example, page 11, lines 3-8, of the specification, in which the use of biomolecules other than oligonucleotides is supported.

Applicants submit that this rejection is rendered moot by the cancellation of Claims 1-4. In new Claims 7-12, which replace cancelled Claims 1-4, the phrase "a series of selected biomolecules" replaces the phrase "multiple kinds of biomolecules." Applicants submit that the new claim wording avoids the Examiner's rejection by pointing out with particularity and clarity that these claims encompass, for example, an arrayed library of related biomolecules that may be of one type, yet may still be a series of different forms of that biomolecule (e.g., a library of different oligonucleotides or proteins). Support for the approach of the new claim wording may be found at page 14, ¶ 1, particularly lines 9-15.

Accordingly, Applicants request that the rejection be withdrawn.

**b.** Claims 5 and 6 are each rejected as indefinite in the recitation "multiple kinds of detecting bodies" for similar reasons to those noted in (a) above.

The Examiner's suggestion that the phrase "labeled sequences of oligonucleotides" be used in place of the objected-to phrase is gratefully acknowledged. However, Applicants assert that the rejection is rendered moot by the cancellation of Claims 5 and 6. In new Claims 13-17, which

replace cancelled Claims 5 and 6, the phrase "a series of detecting bodies" replaces the previous recitation of "multiple kinds of detecting bodies." Applicants assert that the new wording clearly and particularly sets forth that the detecting bodies may a series of different forms of one particular type of biomolecule.

Accordingly, Applicants request that the rejection be withdrawn.

c. Claims 1-6 are rejected as being indefinite in the recitation "the biomolecules are arrayed and fixed on the stimuable phosphor sheet" because it is allegedly unclear whether the biomolecules physically contact the phosphor sheet or are merely "arrayed and fixed" on some surface above the sheet.

The Examiner's suggestion that the claims be amended to clarify, e.g., "wherein the biomolecules are fixed by covalent bonding to the poly-L-lysine coated phosphor sheet," is gratefully acknowledged. A similar wording has been adopted in new dependent Claims 9 and 20. However, Applicants note that the specification discloses the fixing of the biomolecules in several ways: on the surface of a protective layer covering the phosphor layer and coated with poly-L-lysine (p. 14, lines 1-15

and p.16, lines 22-25); within the surface of a permeable protective layer covering the phosphor layer (p. 17, line 25 - p. 18, line 2); on the surface of the phosphor layer itself (p. 17, lines 3-6); and within the phosphor layer itself (p. 17, lines 6-11). These alternatives were clearly recited in cancelled Claims 2 and 3.

To more particularly, clearly and specifically claim the invention, new Claims 11-17 recite in separate independent claims two different modes of fixing of biomolecules: to a phosphor layer and to a protective layer. Claims 1-3 and 5 as originally filed correspond to new Claims 7, 8 and 13. In addition, new Claim 14 recites the use of the protective layer with the detecting bodies. Applicants submit that the new claims clarify with particularity the surface to which the biomolecules or detecting bodies are affixed. Accordingly, Applicants request that the rejection be withdrawn.

d. Claim 4 is rejected as indefinite because the claim is drawn to a method for analyzing a biomolecule but the method allegedly does not recite any method steps of analyzing the biomolecule. The Examiner's suggestion that the claim be amended to recite positive and active steps of analyzing based

on the disclosure of the specification at p. 16, lines 15-21, is gratefully acknowledged.

Claim 4 as originally filed corresponds to new Claim 11, which affirmatively sets forth the suggested positive and active steps for analyzing the biomolecule in compliance with the Examiner's suggestion (see Claim 11, steps iii-vii). In this regard, Applicants also draw the Examiner's attention to new Claims 12 and 17, which correspond to Claim 11 but recite the use of a protective sheet. In view of the positive and active steps recited for analyzing the biomolecule in the new claims, Applicants request that this rejection be withdrawn.

New dependent Claims 18-20 are directed to preferred embodiments of the methods.

e. Claim 4 is rejected as being indefinite in the recitation "causing the stimuable phosphor sheet to store energy" because "causing" is allegedly a non-descriptive activity and therefore it is unclear how the sheet stores energy. The Examiner's suggestion that the claim be amended to clarify, e.g., replace "causing" with "exposing the phosphor sheet to visible light and placing in a dark place to thereby cause," based on the disclosure of the specification at p. 15, lines 11-17, is gratefully acknowledged.

In new Claims 11 and 12, the objected-to step is broken into two separate steps as follows:

(iii) exposing the resulting micro array of step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy released from the energy generating substance.

Applicants submit that new Claims 9 and 10 are in accord with the Examiner's suggestion and point out with particularity and clarity the step by which the phosphor layer stores energy.

Accordingly, Applicants request that this rejection be withdrawn.

f. Claim 6 is rejected as being indefinite because the claim is drawn to a method for analyzing a sample but allegedly the method does not recite any method steps of sample analysis. The Examiner's suggestion that the claim be amended to recite positive and active steps of analyzing based on the disclosure of the specification at p. 16, lines 15-21, is gratefully acknowledged.

New Claims 16 and 17 replace cancelled Claim 6, and, in accord with the Examiner's suggestion, include the following

final step: "determining the identity of a labeled constituent of the sample by comparing the location of the detected signal in the micro array to the location of said one or more members of the selected detecting bodies based on previously stored positional information."

Applicants submit that new Claims 16 and 17 point out with particularity and clarity the active method steps for sample analysis.

Applicants therefore request that this rejection be withdrawn.

g. Claim 6 is rejected as being indefinite in the recitation "causing the stimuable phosphor sheet to store energy" because "causing" is allegedly a non-descriptive activity and therefore it is unclear how the sheet stores energy. The Examiner's suggestion that the claim be amended to clarify how the sheet stores energy, based on the disclosure of the specification at p. 15, lines 11-17, is gratefully acknowledged.

New Claims 16 and 17 replace cancelled Claim 6. As described above in section (e) in relation to new Claim 11, new Claims 16 and 17 also recite the two relevant separate energy storing steps as follows:

(iii) exposing the resulting micro array from step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy release from the energy generating substance,

Applicants submit that new Claim 16 is in accord with the Examiner's suggestion and that it points out with particularity and clarity the step by which the phosphor layer stores energy. Accordingly, Applicants request that this rejection be withdrawn.

**h.** Claims 1-6 are rejected under 35 U.S.C. §112, second paragraph as omitting the allegedly essential elements of a polyester substrate, a phosphor layer comprising a binder and BcFX phosphor particles, and protective layer. The Examiner states that the omitted elements are essential elements in the claimed microarray, or arranged and fixed biomolecules, because without the omitted elements, the claims do not distinctly describe the invention.

Applicants agree with the Examiner that elements needed to distinctly describe the invention must be included in the claims. However, in the present application, Applicants



respectfully traverse the rejection on the grounds that certain of the elements listed by the Examiner are not essential for distinctly claiming the invention.

First, Applicants assert that there is no requirement that the phosphor layer overlay a polyester substrate. New Claims 7-17 all recite a "phosphor layer provided on a substrate," but there is no requirement that the substrate be made of polyester. The substrate merely provides physical support to the phosphor layer and therefore many materials other than polyester may be used as was known to those of skill in the art at the time of filing the present application. For example, Shiraishi et al. (U.S. Patent 4,617,468) at columns 7, lines 36-55 discloses many alternative substrate materials. However, new Claim 15 is added herein as a dependent claim directed to a polyester substrate.

Second, Applicants assert that the phosphor layer is not limited to a composition comprising a binder and a BcFX phosphor particles. The phosphor layer may be constructed of many materials known to those of skill in the art at the time of filing. For example, Shiraishi et al. (U.S. Patent 4,617,468) at columns 8-10 discloses many alternative phosphor compositions.

Third, Applicants have added recitation of the protective layer only to Claims 12, 14 and 17. The protective layer is optional because the biomolecules or detecting bodies may be affixed to the phosphor sheet directly (see, e.g. p.7, ¶ 3, p. 9, lines 14-16 of the specification, and withdrawn Claim 3). Consequently, the protective layer is now recited in Claims 12, 14 and 17 to particularly and clearly claim it as one possible embodiment of the present invention.

Applicants therefore assert that the new claims render moot this rejection because they point out with particularity those elements that are essential for distinctly claiming the invention: other elements are not essential for distinctly claiming the invention and therefore may be omitted or may occur only in certain claims.

Accordingly, Applicants request that this rejection be withdrawn.

## **II. Rejection of claims under 35 U.S.C. § 102**

At page 4 of the Office Action, Claims 1-3 and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Shiraishi et al. (U.S. Patent No. 4,617,468).

The Examiner states that the claims of the present invention are drawn to a microarray comprising a stimulable

phosphor sheet and multiple kinds of biomolecules arrayed and fixed on the phosphor sheet. The Examiner states that the claims are given their broadest reasonable interpretation consistent with the alleged indefinite claim language discussed above, and the description of a microarray embracing a macroarray.

Regarding claim 1, the Examiner asserts that Shiraishi et al. discloses a microarray comprising a stimuable phosphor sheet, and multiple kinds of biomolecules arrayed and fixed on the stimuable phosphor sheet (col. 5, lines 53-65; col. 13, lines 26-35).

Applicants traverse the rejection. Shiraishi et al. discloses a stimuable phosphor sheet onto which a support medium such as an electrophoresis gel can be adhered, for example for use in autoradiography. A mixture containing radioactively-labeled substances can be resolved in the support medium, either before or after the support medium is adhered to the phosphor sheet.

The invention of Shiraishi et al. is quite distinct from the invention of Claims 1-3 and 5, which correspond to new Claims 7, 13 and 14. As noted by the Examiner above, instant Claim 1 clearly recite a phosphor sheet with biomolecules

arrayed and fixed thereto. Thus, the claims clearly state that the biomolecule (or detecting body) is fixed on, or within, the phosphor layer or protective layer, as opposed to being fixed on, or within, a substrate placed on top of the phosphor layer or protective layer.

Thus, Shiraishi et al. cannot anticipate the rejected claims or new Claims 7-20, because Shiraishi et al. does not disclose at least one of the elements of those claims: the element that the biomolecules or detecting bodies are affixed to the phosphor layer (Claims 7, 11, 13 and 16) or the protective layer (Claims 8, 12, 14 and 17).

Accordingly, Applicants request that this rejection be withdrawn.

### III. Rejection of claims under 35 U.S.C. § 103(a)

At page 5 of the Office Action, paragraph 6, Claims 4 and 6 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shiraishi et al. in view of Davis et al. (Basic Methods in Molecular Biology).

It appears to be the Examiner's position that Shiraishi et al. teaches the steps recited in Claims 4 and 6, but does not teach labeling the fixed biomolecule by hybridization with a labeled biomolecule. However, the Examiner contends that

labeling a biomolecule by hybridization with a labeled biomolecule was well known in the art at the time of the invention as taught by Davis et al. Thus, the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the labeling of Shiraishi et al., using the teaching of Davis et al.

Applicants traverse. As described in section II above, Shiraishi et al. lacks at least one element of the rejected claims, which is the affixing of the biomolecule or the detecting body to the phosphor sheet or protecting layer. Thus, Shiraishi et al. does not provide all the elements of new Claims 7-20. A *prima facie* case of obviousness requires that the combined references teach or suggest all of the claim limitations. Davis et al. does not cure the deficiency in Shiraishi et al. because Davis et al. only teaches hybridization and not the affixing of biomolecules or detecting bodies to the phosphor sheet or protecting layer of the present invention. Accordingly, the combination of Shiraishi et al. and Davis et al. does not teach or suggest all the elements of the rejected claims, as required to establish a *prima facie* case of obviousness.

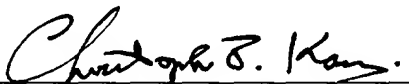
Accordingly, Applicants request that this rejection be withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-6 are canceled.

Claims 7-20 are added as new claims.

7. (New) A micro array, comprising a stimuable phosphor layer provided on a substrate, wherein said phosphor layer has affixed thereto an array of a series of selected biomolecules.

8. (New) A micro array, comprising a stimuable phosphor layer provided on a substrate and a protective layer provided on said stimuable phosphor layer, wherein said protective layer has affixed thereto an array of a series of selected biomolecules.

9. (New) The micro array of claim 8, wherein said biomolecules are affixed by bonding to a poly-L-lysine coated protective layer.

10. (New) The micro array of claims 7 or 8, wherein said biomolecule is an oligonucleotide.

11. (New) A method for analyzing a biomolecule, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate,

wherein said phosphor layer has affixed thereto an array of a series of selected biomolecules,

(ii) contacting the micro array of step (i) with a labeled biomolecule, to cause the labeled biomolecule to be bound to one or more members of the series of selected biomolecules, wherein said labeled biomolecule is labeled with an energy generating substance,

(iii) exposing the resulting micro array of step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy released from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect the one or more members of the series of selected biomolecules which are bound to the labeled molecule, and

(vii) determining the identity of the one or more members of the series of selected biomolecules bound to the labeled



biomolecule by comparing the location of the detected signal in the micro array to the location of said one or more members of the series of selected biomolecules based on previously stored positional information.

12. (New) A method for analyzing a biomolecule, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate and a protective layer provided on said phosphor layer, wherein said protective layer has affixed thereto an array of a series of selected biomolecules,

(ii) contacting the micro array of step (i) with a labeled biomolecule, to cause the labeled biomolecule to be bound to one or more members of the series of selected biomolecules, wherein said labeled biomolecule is labeled with an energy generating substance,

(iii) exposing the resulting micro array of step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy released from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect the one or more members of the series of selected biomolecules which are bound to the labeled molecule, and

(vii) determining the identity of the one or more members of the series of selected biomolecules bound to the labeled biomolecule by comparing the location of the detected signal in the micro array to the location of said one or more members of the series of selected biomolecules based on previously stored positional information.

13. (New) A micro array, comprising a stimuable phosphor layer provided on a substrate, wherein said phosphor layer has affixed thereto an array of a series of selected detecting bodies.

14. (New) A micro array, comprising a stimuable phosphor layer provided on a substrate and a protective layer provided on said stimuable phosphor layer, wherein said protective layer has affixed thereto an array of a series of selected detecting bodies.

15. (New) The micro array of any one of claims 7, 8, 13 or 14, wherein said substrate is polyester.

16. (New) A method for analyzing a sample, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimuable phosphor layer provided on a substrate, wherein said phosphor layer has affixed thereto an array of a series of selected detecting bodies,

(ii) contacting the micro array of step (i) with a sample, wherein said sample comprises a plurality of constituents which are labeled with an energy generating substance, to cause a constituent in said sample to be bound to one or more members of the series of selected detecting bodies,

(iii) exposing the resulting micro array from step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy release from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect a labeled constituent of the sample which is bound to a detecting body, and

(vii) determining the identity of a labeled constituent of the sample by comparing the location of the detected signal in the micro array to the location of said one or more members of the selected detecting bodies based on previously stored positional information.

17. (New) A method for analyzing a sample, comprising the steps of:

(i) preparing a micro array, wherein said micro array comprises a stimulable phosphor layer provided on a substrate and a protective layer provided on said phosphor layer, wherein said protective layer has affixed thereto an array of a series of selected detecting bodies,

(ii) contacting the micro array of step (i) with a sample, wherein said sample comprises a plurality of constituents which are labeled with an energy generating substance, to cause a constituent in said sample to be bound to one or more members of the series of selected detecting bodies,

(iii) exposing the resulting micro array from step (ii) to visible light to thereby induce the release of energy from phosphor molecules in the stimuable phosphor layer,

(iv) placing the micro array of step (iii) in a dark place to thereby cause the stimuable phosphor layer to store energy release from the energy generating substance,

(v) exposing the resulting micro array of step (iv) to stimulating rays which cause the stimuable phosphor layer to emit light in proportion to the amount of energy stored therein,

(vi) photoelectrically detecting the resulting emitted light from step (v) as a signal, so as to detect a labeled constituent of the sample which is bound to a detecting body, and

(vii) determining the identity of a labeled constituent of the sample by comparing the location of the detected signal in the micro array to the location of said one or more members of the selected detecting bodies based on previously stored positional information.

18. (New) The method of any one of claims 11, 12, 16 and 17, wherein said substrate is polyester.

19. (New) The method of claim 11 or 12, wherein said biomolecules are oligonucleotides.

20. (New) The method of claim 12, wherein said biomolecules are affixed by bonding to a poly-L-lysine coated protective layer.